

REMARKS

The Official Action of May 18, 2005, and the prior art cited and relied upon therein have been carefully reviewed. The claims in the application remain as claims 1-19, and these claims define patentable subject matter warranting their allowance. Accordingly, applicant respectfully requests favorable reconsideration and allowance.

Acknowledgement by the PTO of the receipt of applicant's papers filed under Section 119 is noted.

The benefit information has now been inserted into applicant's specification at the top of page 1 of the specification, as helpfully suggested by the examiner. For the record, however, such information is adequately presented in an application data sheet (ADS) as was filed in the present application.

Applicant appreciates the Examiner's commentary about an Information Disclosure Statement (IDS) in paragraph 4 of the Official Action, which applicant understands is a "boiler plate" paragraph. Applicant notes for the record that all references cited in the specification have been listed on a PTO form-Sb/08A, namely as references AA, AC, AD-AF and AI.

Claims 1-19 have been objected to as using the acronym PAF. Applicant thanks the examiner for the helpful suggestion in this regard, and has adopted same by defining the first instance of PAF, i.e. in claim 1. This amendment is supported in applicant's specification for instance at page 1, paragraph [0002].

Applicant understands that, consistent with the examiner's commentary and also what was done in the parent application, it is not necessary to change "PAF" in the remaining claims.

Withdrawal of the objection is respectfully requested.

Claims 1-19 have been rejected under the second paragraph of §112 as being indefinite. This rejection is respectfully traversed.

In paragraph 7A, the examiner objects to the use of the term "early". Applicant respectfully disagrees that this term is indefinite. In the parent application, applicant pointed out that the term "early atherosclerosis" is described in the application, and applicant submitted a publication in the name of Skalen et al (duplicate copy previously attached) appearing in Nature, showing that the term "early atherosclerosis" is a conventionally used term within the field.

Thus, the term "early atherosclerosis" is well known. It is described in Applicant's Specification in paragraph [0002] on page 1 under the heading "Background of the Invention".

Also the term "early vascular dysfunction and/or vascular disease" is mentioned in the application, see page 3, paragraph [0005] and page 5, paragraph [0010]. The term "early" refers to the very first stages of the dysfunction or disease when it is yet not easily detected by other methods and has not given rise to noticeable disease. Attached are two, out of many, medical articles published on the web, showing that the term "early" is a well established term within the field.

The present Specification is directed to those skilled in the art, and those persons know what is meant by "early atherosclerosis". The term was accepted in the parent application (see claim 2 in the parent patent), and should be accepted in the present application.

Claim 2 has been rejected for the use of the term "utilizes" as being vague and indefinite. Claim 2 has been amended above to replace the objected terminology with the term "comprises". The amendment is supported by the description at page 7, paragraph [0015].

Claims 2, 5-7 and 10 have been amended above to change the terminology "capable of binding" to "that binds".

Applicant disagrees that the claims as previously drafted are indefinite, and considers the above amendments to be of a formal nature only, i.e. made to place the claims in better form consistent with the Examiner's understanding of what is necessary or desirable under U.S. practice. The amendments are not "narrowing" amendments because the scope of the claims has not been reduced. No limitations have been added and none are intended.

Applicant respectfully maintains that the claims as previously drafted, considered in light of Applicant's Specification (fully consistent with the law), would not have been confusing to those skilled in the art, and therefore the claims in their previous form are fully in accordance with §112. At **worst**, these claims amended above, as previously drafted, might be considered objectionable, but **only** as to form.

In paragraph 7D, the examiner rejects claim 4, it being the examiner's position that it is not clear how a diagnosis of cardiovascular disease will also determine independent disorders like early atherosclerosis, hypertension and thrombosis.

According to the literature, cardiovascular disease (CVD) refers to all diseases and conditions involving the heart and blood vessels, including stroke, which is a common cause of **thrombosis**. The underlying cause of most CVD is a gradual clogging of the arteries (**atherosclerosis**) that supply blood to the heart, brain, and other vital organs. Cardiovascular diseases further include arteriosclerosis, coronary artery disease, heart valve disease, arrhythmia, heart failure, **hypertension**, orthostatic hypertension, shock, endocarditis, diseases of the aorta and its branches, disorders of the peripheral vascular system, and congenital heart disease.

Therefore, while applicants' claimed kit **does not** distinguish early atherosclerosis, hypertension and thrombosis from other cardiovascular diseases, as stated by the examiner, **they are included in the term**, i.e. a patient suffering from one of these conditions can use applicant's kit and the condition will be uncovered. Moreover, please note that a similar formulation was approved in the parent application (claim 2) thereof.

Applicant respectfully requests withdrawal of the rejections under the second paragraph of §112.

Claims 1-19 have been provisionally rejected on the basis of obviousness-type double patenting over claim 12-23 of

copending application 10/814,194, in view of Ostermann et al.

This rejection is respectfully traversed.

Claims 12-23 in applicant's co-pending application 10/814,194 have been deleted by preliminary amendment filed in said co-pending application.

Applicant respectfully requests withdrawal of the rejection.

Claims 1, 2 and 5-7 have been rejected under §103 as obvious from Barquinero et al, Ref AC, (Barquinero) in view of Foster et al USP 4,444,879 (Foster). This rejection is respectfully traversed.

Applicant agrees that Barquinero does not anticipate applicant's claims. In this regard, Barquinero mentions that serum from a patient with thrombotic manifestations showed high specific binding to PAF. Thus, this teaching does not imply that antibodies against PAF (aPAF) may be used to diagnose or predict vascular disease because the patient **already had** thrombotic manifestations when this specific binding was demonstrated.

Furthermore, Barquinero also mentions aCL, in addition to aPAF, and there is nothing indicating that only aPAF should be used.

The stated objects in Barquinero and the present invention are different. There is nothing in the Barquinero

publication indicating that antibodies against PAF could be used as a **risk estimation** instrument for assessing the risk of developing vascular disease.

The rejection states that Barquinero uses "blood sample from patients with systemic lupus erythematosus (SLE)" and that "SLE includes blood vessel inflammation, which could lead to cardiovascular disease (risk)".

But lupus is a condition of chronic inflammation caused by an autoimmune disease. Autoimmune diseases are of course illnesses which occur when the body's tissue are attacked by its own immune system. The immune system is a complex system within the body that is designed to fight infectious agents, for example bacteria and other foreign invaders. One of the mechanisms that the immune system uses to fight infections is the production of antibodies. Patients with lupus produce abnormal antibodies in their blood that target tissues within their own body rather than foreign infectious agents.

Lupus can cause diseases of the skin, heart, lungs, kidneys, joints, and nervous system. When only the skin is involved, the condition is called discoid lupus. When internal organs are involved, the condition is called systemic lupus erythematosus. It is true that SLE secondarily could lead to cardiovascular disease. However, not only the heart

is affected by the abnormally high production of antibodies, but several other internal organs are affected as well.

It is therefore not at all obvious to conclude from the teachings in Barquinero that PAF is an instrument to evaluate if the patient is at risk for developing cardiovascular disease simply because the patient is diagnosed with SLE. According to Barquinero, patients with antiphospholipid antibodies were subjects of a study involving 148 patients with autoimmune diseases, of which 120 patients were diagnosed with SLE, and 28 had primary antiphospholipid syndrome. Further 20 patients suffering from syphilis were studied. There is no other information disclosed or even suggested in Barquinero which would have given guidance to another application than the one described and summarized in the Barquinero abstract.

Regarding the assertion that it would have been obvious to construe a kit for the diagnosis of the above-mentioned disease in view of Foster, applicant strongly disagrees. First, the kit disclosed in Foster is used for a completely different purpose and does not mention for instance the diagnosing of cardiovascular disease or the use of aPAF. A person of ordinary skill in the art would therefore not turn to Foster for guidance as how to construct a kit as in the present invention.

Further, a kit for diagnosing a disease, with all its advantages, is not something that the skilled person readily even contemplates, let alone constructs, as soon as a method for diagnosing the disease is known. A kit comprises further means than just e.g. a reagent and a coated ELISA-plate, but are most often accompanied by controls and a description as how to interpret the results and how said results provide information for the diagnosing of the disease, for instance the diagnosing of cardiovascular disease or spontaneous abortion.

Therefore, the kit as claimed in the present application could not have been construed and accomplished without any inventive skill, and especially since the method of diagnosing the disease was completely unknown until the kit was conceived. Moreover, the kit of the present invention is extremely useful since it can be used to diagnose a number of disease and conditions related to the presence of aPAF.

Moreover, even if Foster were obviously combinable with Barquinero, contrary to applicant's strong traversal above, the combination would still not reach any of applicant's claims because Foster does not make up for the deficiencies of Barquinero as pointed out above, and indeed has not even been cited for that purpose.

Withdrawal of the rejection is in order and is respectfully requested.

Claims 3, 4 and 8-10 have been rejected as obvious under §103 from Barquinero in view of Foster and further in view of Ostermann et al, reference AJ (Ostermann). This rejection is respectfully traversed.

First, the rejection relies on the obviousness of the combination of Barquinero in view of Foster which has been traversed above. Ostermann has not been cited to make up for the deficiencies in the proposed combination of Barquinero in view of Foster, and indeed does not do so. Accordingly, claims 2, 4 and 8-10 are patentable for the reasons given above, regardless of the addition of Ostermann.

Regarding Ostermann, the examiner has (respectfully) once again confused the issue of aPAF as compared to PAF. Ostermann teaches measuring of PAF levels in serum and plasma from patients suffering from coronary artery disease. While it is true that Ostermann further teaches that PAF could be used to discriminate between low and high risk groups of patients, it is also true (and clear) that Ostermann does not measure aPAF but instead PAF itself; and there is no data or information whatsoever suggesting or even indicating to a person skilled in the art that aPAF and PAF are closely

related at all. The present invention is by no means intended to be a surrogate of PAF-levels.

Withdrawal of the rejection is respectfully requested.

Claims 11-18 have been rejected as obvious under §103 from Barquinero in view of Foster and further in view of Karasawa et al, reference AH, (Karasawa). This rejection is respectfully traversed.

The deficiencies of Barquinero and Foster have been discussed above. Karasawa has not been cited to make for these deficiencies, and indeed does not do so. Therefore, the claims define non-obvious subject matter regardless of Karasawa.

Karasawa shows that aPAF exhibits very low crossreaction with lyso-PAF and lyso-phosphatidylcholine, in fact less than 0.025%. Moreover, claim 1 refers to antibodies against PAF, and/or antibodies against an antigen than binds to aPAF. Dependent claims 11-18 refer to phospholipids comprised of said antigens that binds to aPAF. As applicant has shown above that claim 1 is novel and unobvious with regard to the cited prior art, claims 11-18 should be allowed as well.

Withdrawal of the rejection under §103 is in order and is respectfully requested.

Claim 19 has been rejected under §103 as being obvious from Barquinero in view of Foster, further in view of Ostermann, as applied to claims 3, 4 and 8-10 above, and further in view of Karasawa. This rejection is respectfully traversed.

The deficiencies of Barquinero, Foster, Ostermann and Karasawa have been pointed out above. Thus, the references, even in the extremely unlikely event that a person having ordinary skill in the art might be able to cobble together features from such four distinct references, vigorously disputed by applicant, in any resultant combination would still not reach even the main claim 1 (let alone claim 19 which incorporates claims 10 and 1) because of the aforementioned deficiencies in Barquinero, which deficiencies are not overcome by any of the other citations.

The applicant submits that withdrawal of the rejection is in order, and such is respectfully requested.

The other prior art documents of record and not relied upon have been noted, along with the implication that such documents are deemed by the PTO to be insufficiently pertinent to warrant their application against any of applicant's claims.

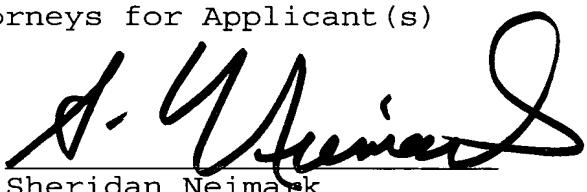
Appln. No. 10/814,195
Amd. dated August 2, 2005
Reply to Office Action of May 18, 2005

Applicant believes that all issues raised in the Office Action have been addressed above in a manner favoring patentability. Favorable reconsideration and allowance are earnestly solicited.

Respectfully submitted,

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